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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/820,307 | 04/08/2004 | Barry S. Brown | DM-7029 DIV | 7454 |

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| EXAMINER | |
|---|---|
| GUCKER, STEPHEN | |
| ART UNIT | PAPER NUMBER |
| 1649 | |

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/820,307 | BROWN ET AL. | |
| | Examiner | Art Unit | |
| | Stephen Gucker | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on 4/8/04

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☑ The drawing(s) filed on 4/8/04 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 7/12/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 7, 12, and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. While claim 1 recites methods of evaluating a compound for utility in treating neurological disease based on its ability to: 1) increase or agonize, or 2) decrease or antagonize, the activity of the potassium channel, dependent claims 7, 12, and 18 attempt to limit the independent claim further by reciting wherein the compound is an agonist of the potassium current. However, for the dependent claims to truly limit the scope of the base claim upon which it depends, it would be necessary to know *a priori* what the function of the compound would be in terms of its effect on the recited potassium channel. In other words, to simply test a compound for agonism without knowing it is an agonist beforehand (as required by claims 7, 12, and 18) would not be a further limitation of claim 1, and therefore the testing of a compound whose potential agonism was unknown, by claim construction analysis, would be outside the scope of claims 7, 12, and 18 (but not of claim 1). While the specification does provide an adequate written description of evaluating known antagonists of the M-type potassium current (which is taught by the instant specification

to be the same as the KCNQ2/KCNQ3 potassium current (page 3, lines 4-11)), it does not provide an adequate written description of even a single specific species of M-type potassium current agonist, nor does it describe a specific method by which a known single specific species of M-type potassium current agonist can be used in the instant method to increase the activity of the potassium channel. The grounds of this rejection could be obviated by canceling claims 7, 12, and 18 and by adding a new independent claim that recited, "A method of evaluating a compound for utility in treating neurological disease by acting as an agonist at a potassium channel comprising contacting a compound with a cell that coexpresses KCNQ2 and KCNQ3, wherein the KCNQ2 and the KCNQ3 form a potassium channel; and measuring any agonist activity of the compound on said potassium channel."

**3.** The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**4.** Claims 1-2, 5-6, and 8 are rejected under 35 U.S.C. § 102(a) as being anticipated by Yang et al. (*JBC, 273(31):19419-19423*, "Yang"). Yang teaches methods of functional coexpression of hKCNQ2 and hKCNQ3 in *Xenopus* oocytes and identifies these potassium channels as being responsible for benign familial neonatal convulsions

(BFNC), a form of epilepsy (abstract, pages 19419, 19421-19422, and Figure 3). The known antagonistic compounds TEA and clofilium are identified as antagonists of the potassium current (page 19421).

**5.** Claims 1, 3, 8, 11, and 13-14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lamas et al. (*Eur. J. Neurosci., 9:605-616, 1997*, "Lamas"). Lamas teaches a method that demonstrates the antagonism of M-type potassium current in rat superior cervical ganglion cells (abstract and pages 608-609) by the antagonist linopirdine, and suggests that linopirdine might have beneficial therapeutic effects in diseases associated with defects in cognition, such as Alzheimer's disease (page 605). M-type potassium current is described in the instant specification as being the joint product of KCNQ2 and KCNQ3 potassium channels, and that they are antagonized by linopirdine (page 1, line 30 to page 3, line 11).

**6.** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**7.** Claims 1, 3-6, 8, 11, 13-14, 17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Yu et al. The teachings of Yang are as set forth in **¶4** above. Yang does not teach coexpressing hKCNQ2 and hKCNQ3 in mammalian CHO cells. Yu recommends the use of CHO cells in methods employing exogenous potassium channel expression. It would have been obvious at the time of the invention for one of ordinary skill in the art to coexpress the hKCNQ2 and hKCNQ3 of Yang in the CHO cells of Yu because Yu explicitly suggests the use of CHO cells to study exogenous potassium channel expression because little or no potassium current is found in CHO cells if the CHO cells are not transfected with nucleic acid encoding for potassium channels. Yu states that "CHO cell lines are a preferred system for exogenous K+ [potassium] channel expression" (last sentence of abstract), rendering the instant claims *prima facie* obvious.

**8.** Claims 1 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Siegel et al. (*Neuron, 19:735-741, 1997,* "Siegel"). The teachings of Yang are as set forth in **¶4** above. Yang does not teach methods using voltage sensitive dyes detectable by fluorescence. Siegel does teach methods using a modified green fluorescent protein (GFP) fused to a potassium channel to measure transmembrane voltage in single cells (abstract and Figures 2-4). It would have been obvious at the time of the invention for one of ordinary skill in the art to coexpress the hKCNQ2 and

hKCNQ3 of Yang, fused to the GFP of Siegel, because Siegel explicitly states that "a voltage sensor encoded into the DNA has the advantage that it may be introduced into an organism noninvasively and targeted to specific developmental stages, brain regions, cell types, and subcellular compartments" (last sentence of abstract). Another advantage of the fused GFP of Siegel is that it "makes single spikes 30 times easier to detect than they would be with a fast dye with a comparable fractional fluorescence change" (page 740), rendering the instant claims *prima facie* obvious.

**9.** Claims 1, 11, 13-17, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Siegel et al. and further in view of Yu. The teachings of Yang, Siegel, and Yu are as set forth in **¶4, ¶8,** and **¶7**, respectively. Yang does not teach methods using voltage sensitive dyes detectable by fluorescence or coexpressing hKCNQ2 and hKCNQ3 in mammalian CHO cells. Siegel does teach methods using voltage sensitive dyes detectable by fluorescence, but does not teach the use of mammalian CHO cells. Yu teaches the use of CHO cells to study exogenous potassium channel expression. It would have been obvious at the time of the invention for one of ordinary skill in the art to coexpress the hKCNQ2 and hKCNQ3 of Yang, fused to the GFP of Siegel in the CHO cells of Yu because of the combined advantages and suggestions set forth individually by Siegel (single spikes 30 times easier to detect) and Yu (no endogenous potassium channels in CHO cells to complicate results), and because Siegel explicitly teaches that "while we have not tested FlaSh [potassium channel-GFP chimera] in mammalian cells, we expect it to work just as well, given the high levels of expression of both Shaker [potassium channel] and GFP in a variety of

mammalian cell lines" (page 738). Thus, Siegel is explicitly teaching a high expectation of success, rendering the instant claims *prima facie* obvious.

**10.** No claim is allowed.

**11.** Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached at (571) 272-0867. The fax phone number for this Group is currently (571)-273-8300.

Stephen Gucker

October 16, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER